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| 13. ABSTRACT (Maximum 200 Words) This research project will build upon the Long Island Breast Cancer Study Project (LIBCSP), a large population-based, case-control study of the environment and breast cancer. Participants completed an in-person interviewer-administered interview, donated blood and urine samples and had home environment samples (dust, soil and water) collected. For this study, 200 cases and 200 controls who donated urine samples will be selected and their urine samples will be analyzed for a panel of EE biomarkers. In addition, these same women will be screened for polymorphisms in both the estrogen receptor alpha and beta genes. Breast cancer risk in relation to the combination of these multiple EE exposures and gene-environment interaction will be investigated using sophisticated statistical methods such as hierarchical regression models and factor analysis. Additionally, a pilot investigation of the correlation between EE levels in house dust and urinary biomarker levels will be conducted. Currently, samples for this study have been selected and the laboratory analyses are underway. Results of the proposed research project will be of enormous public health relevance since they may advance our knowledge of modifiable breast cancer risk factors and newly identified EEs, thereby providing information that is essential for primary prevention. | | | | |
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Introduction

The primary aim of the multidisciplinary postdoctoral award is to position Dr. Teitelbaum as an independent research scientist specializing in the environmental and molecular epidemiology of combined effects of multiple exposures. The research aims – relating multiple environmental estrogen exposure to breast cancer risk – will be examined in the Long Island Breast Cancer Study Project, a large population-based case-control study of breast cancer and the environment.

Specific Aims:

- To investigate whether women with higher combined exposure levels to multiple environmental estrogens are at increased risk of breast cancer.
- To investigate the possibility that women who carry adverse alleles in the estrogen receptor alpha and beta genes and have higher combined exposure levels to multiple environmental estrogens are at higher risk of breast cancer than women without these alleles.
- To evaluate the relationship between household dust and urinary levels of environmental estrogens.

Body

Below I have detailed the training and research that has been completed over the past year according to the tasks outlined in the Statement of Work.

Task 1. To undertake the proposed training program (Months 1-36):

- a. Complete graduate coursework in biostatistics, genetics, and pharmacology
 - Completed intensive toxicology course entitled “Reproductive, Developmental and Endocrinologic Toxicology” at the Mailman School of Public Health, Columbia University, August 2004.
 - Attended an intensive short course in advanced statistical methods, “Using Random Forests for Scientific Discovery,” and two biometry tutorials “Tools and Tips for Handling Good Data With Bad Properties: Analytic Approaches for Health Care Cost, Occupational/Environmental Exposure, and Biomarker Data in the Real World” and “Sample-Size Analysis in Study Planning with SAS PROCs POWER and GLMPOWER: Concepts and Issues, with In-Depth Examples” at the Annual meeting of the International Biometric Society - Eastern North American Region, March 2005.
 - Accepted to The Jackson Laboratory Annual Short Course In Medical And Experimental Mammalian Genetics, July 2005.
- b. Conduct several epidemiologic analyses of multiple environmental exposures
 - Author and co-author on multiple publications (see Reportable Outcomes)
 - Continue to participate in departmental environmental and biometry journal clubs, attend monthly meetings of departmental projects, attend weekly Cancer Center seminars and Mount Sinai grand rounds on endocrinology, breast pathology, and oncology.
 - Attended and presented at the departmental biometry and environmental epidemiology journal clubs.
 - Attended monthly meeting of the NIEHS Center for Children's Environmental Health
 - Attended Cancer Center seminars and grand rounds when topics were relevant to my research and training goals
- c. Become a member of and alternately attend annual meetings of the International Society of Exposure Analysis (ISEA)/International Society for Environmental Epidemiology (ISEE) and Eastern North American Region of the International Biometric Society (ENAR).
 - Current member of:
 - International Society for Environmental Epidemiology
 - Eastern North American Region of the International Biometric Society
 - American Association for Cancer Research (AACR) and Molecular Epidemiology Working Group of AACR
 - Society for Epidemiologic Research
 - Attended professional scientific meetings:
 - International Society of Environmental Epidemiology (ISEE) and presented a poster on “Characteristics associated with residential pesticide use on Long Island, NY”

- American Association for Cancer Research (AACR) and co-chaired mini-symposium on “The endogenous and exogenous effects of hormones on breast and prostate cancer”
- Annual meeting of the International Society for Exposure Analysis (SEA)
- Emerging Topics in Breast Cancer and the Environment
- d. Complete an internship in the lab conducting genetic screening to gain an appreciation for laboratory work commonly performed in molecular epidemiology studies.
 - Accepted to attend the New England Biolabs course in Molecular Biology and PCR, June 2005. This is an intensive two-week course that will provide the required training through theoretical and practical lab work training.
- f. Regularly meet with my mentors and advisors to oversee my progress and research development.
 - Met both formally and informally with Dr. Wolff each week to review progress, discuss issues related to conducting research and professional development.
 - Met with other mentors and advisors on an “as needed” basis depending on the specific research issue requiring discussion

Task 2. To conduct a case-control study of combined environmental estrogen exposure, the estrogen receptor alpha and estrogen receptor beta genes and breast cancer (Months 1-30):

- a. Conduct sample selection for urinary biomarkers (200 cases and 200 controls) and dust analysis (50 cases and 50 controls)
 - Study subjects have been chosen in consultation with Dr. Sylvan Wallenstein for both analyses.
 - Additional funding has been obtained to increase urinary biomarker sample size.
- b. Conduct urinary biomarker environmental estrogen assays.
 - Several in-person meetings, phone conferences and email communication with collaborators from the CDC (where biomarker assays will be conducted) have been held to establish protocols for sample shipment, analyses and delivery of results.
 - Analyses will be conducted in Year 2 and 3
- c. Conduct screening for estrogen receptor alpha and estrogen receptor beta genetic polymorphisms.
 - Polymorphism screening will be conducted in Year 2 and 3
- d. Conduct house dust environmental estrogen analyses.
 - Dust samples are currently being located in repository freezers and processing/analyses will begin in Year 2
- e. Conduct quality control and verification of data.
 - To be conducted in Years 2 and 3

Task 3. To conduct data analysis, manuscript preparation and dissemination of research results at conferences (Months 31-36)

- To be conducted in Year 3

Key Research Accomplishments

- Designed and oversaw field operations of a methodological study to assess the inter- and intra-person variability of urinary metabolites of the environmental estrogens, including bisphenol A, phthalates and pyrethroid pesticides.
 - The collection of serial urine samples will be completed in April 2005.
 - The CDC has analyzed the first batch of samples and has delivered the biomarker analyte results.
 - Using this preliminary data, an abstract has been submitted for presentation at the 2005 Annual meeting of the International Society of Environmental Epidemiology.

Reportable Outcomes

- Publications

Peer-reviewed articles

Teitelbaum, SL, Calafat, AM, Britton, JA, Silva, MJ, Ye, X, Kuklenyik, Z, Reidy, JA, Brenner, BL, Galvez, MP, Wolff, MS. Temporal variability in urinary phthalate metabolites, phenols and

- phytoestrogens among children. (abstract submitted to International Society of Environmental Epidemiology 2005).
- Wolff MS, Teitelbaum SL, Liou PJ, Santella RM, Wang RY, Jones RL, Caldwell KL, Sjödin A, Turner WE, Li W, Georgopoulos P, Berkowitz GS. 2005. Exposures among Pregnant Women near the World Trade Center Site on 9/11 Environ Health Perspect: doi:10.1289/ehp.7694. [Online 10 February 2005]
- Teitelbaum SL, Gammon MD, Britton JA, Neugut AI, Levin B, Stellman SD. Reported residential pesticide use and breast cancer risk on Long Island, NY. (submitted to Epidemiology – under revision)
- Teitelbaum SL, Gammon MD, Britton JA, Neugut AI, Levin B, Stellman SD, Wolff MS. Characteristics and patterns of residential pesticide use on Long Island, NY. International Society of Environmental Epidemiology. August 2004.
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- Bernstein JL, Haile RW, Bernstein L, Langholz BM, Thomas DC, Stovall M, Malone KE, Lynch CF, Olsen JH, Anton-Culver H, Shore RE, Boice JD, Berkowitz GS, Gatti RA, Teitelbaum SL, Rosenstein B, Borresen-Dale AL, Concannon P, Thompson WD. An Efficient Study Design for Evaluating Gene-Environment Interactions in the Etiology of Breast Cancer: the WECARE Study. Breast Cancer Research. 6(3):R199-214. 2004
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- Kabat GC, O'Leary ES, Schoenfeld ER, Greene JM, Grimson R, Henderson K, Kaune WT, Gammon MD, Britton JA, Teitelbaum SL, Neugut AI, Leske MC; EBCLIS Group. Electric blanket use and breast cancer on Long Island. Epidemiology. 14(5):514-20. 2003.
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Peer-reviewed articles --collaborative authorship

O'Leary ES, Schoenfeld ER, Henderson K, Grimson R, Kabat GC, Kaune WT, Gammon MD, and Leske MC for the EBCLIS Group. Wire coding in the EMF and Breast Cancer on Long Island Study: relationship to magnetic fields. *Journal of Exposure Analysis and Environmental Epidemiology* 2003;13:283-293.

Schoenfeld ER, O'Leary ES, Henderson K, Grimson R, Kabat GC, Ahnn S, Kaune WT, Gammon MD, and Leske MC for the EBCLIS Group. Electromagnetic fields and breast cancer on Long Island: A case-control study. *American Journal of Epidemiology* 2003;158(1):47-58.

Letters

Britton JA, Teitelbaum SL, Wolff MS. "Correspondence re: Schoen et al., Lack of Association between Adipose Tissue Distribution and IGF-1 and IBFBP-3 in Men and Women. *Cancer Epidemiol. Biomark. Prev.*, 11: 581-586, 2002" (Letter). *Cancer Epidemiology Biomarkers and Prevention*. 12:586. 2003.

- Invited plenary session presenter on Breast Cancer and the Environment at the 2004 annual meeting of the Susan G. Komen Foundation.
- Co-leader of workshop on Breast Cancer and the Environment at the 2004 annual meeting of the National Breast Cancer Coalition.
- Invited discussant in a workshop designed to examine how to integrate molecular epidemiologic and human toxicologic studies within the Agricultural Health Study.
- Principal Investigator of NIEHS funded Mentored Scientist Career Development Award.
- Co-Investigator on Project 2 of NIEHS/EPA funded "Breast Cancer and the Environment Research Center" (MS Wolff, PI).
- New investigator award in our department's NIEHS/EPA funded Children's Environmental Health Center.

Conclusions

I have made significant progress towards becoming an independent research scientist specializing in the environmental and molecular epidemiology of combined effects of multiple exposures. I have extended my multiple exposure study opportunities by obtaining 2 additional federally funded initiatives and increased my ability to conduct multiple exposure epidemiologic analyses through the training I have completed. The work accomplished during the first year of this grant has built a strong foundation for completing the proposed research in the remaining years of this project.

"So What"

The research I have conducted thus far is directly related to the goals of my postdoctoral award. All of these urinary metabolites measured in the temporal variability study will be measured in the urine samples of the case-control study analyses that will be conducted in future years of this award. The results will provide invaluable information for the data analysis of the case-control study and contribute to our understanding of how these biomarkers can be best used in epidemiologic studies.

References

None

Appendices

None